REMARKS

I. Claim Status.

Upon entry of this Amendment, claims 14, 19, 20, 25, 51, 52, 55, 56, 59, 60, 63, 64, and 71-92 are pending. All cancelled claims are cancelled without prejudice or disclaimer.

In the Final Office Action, the Examiner noted that the amendment to the claims filed August 10, 2005 was non-compliant with Rule 1.121 because claim 69 was not present within the text of the claim amendment. The instant Amendment lists claim 69 as cancelled. The Amendment is believed to comply with Rule 1.121.

Claims 14, 20, 51, 52, 55, 56, 59, 60, 63, 64, 71, and 72 have been amended, without prejudice or disclaimer as to any subject matter that may have deleted. Claims 73-92 have been added. Support for the claim amendments and newly added claims is found throughout the application as filed, e.g., at page 15, paragraph [0061] et seq., page 8, lines 5-10, page 8, lines 22-31, and the originally filed claims. Support for the particular amyloid β peptides recited in the claims is found in the specification at, e.g., page 8, lines 5-10 (amyloid β carboxyl-termini at position 39, 40, 42, 42, 43 or 44 where position 1 is the aspartate of the amyloid β sequence). Support for the truncated amyloid β peptides recited in claims 77-79, 83-85, 91 and 92 is found in the specification at, e.g., page 8, lines 22-31 (prominent N-terminus truncated Aβ isoforms begin with pyroglutamate at positions 3 and 11 and leucine at position 17).

All claim amendments and new claims are supported by the application as filed. Accordingly, by this Amendment no new matter has been added to the application.

II. Interview Summary.

The Applicants and their representatives wish to thank Examiners Chernyshev and Ulm for the courtesies extended at the personal interview conducted at the Patent and Trademark Office on December 13, 2005. Present at the interview were Dr. Daniel Chain (inventor of the present application) and Applicants' representatives Mitchell Bernstein and Peter Ludwig.

During the interview Dr. Chain presented an explanation of the invention and the benefits of using free-end specific antibodies for inhibiting accumulation of amyloid β in the brain. Dr. Chain explained that the free-end specific antibodies of the invention targeted only

physiologically relevant peptides and that this tended to avoid adverse side effects associated with the use of antibodies that were not free-end specific.

The Schenk and Suzuki references were discussed at some length. The Examiners conceded that Schenk did not disclose the use of free-end specific antibodies. It was agreed that amending the claims to call for free-end specific antibodies would overcome the anticipation rejection based on Schenk.

The Suzuki reference was also discussed during the interview. Applicants' representatives pointed out that Suzuki does not expressly disclose free-end specific antibodies. However, to the extent that certain antibodies disclosed in Suzuki might be free-end specific, those antibodies were disclosed as binding, to peptides that were not physiologically relevant. In contrast, Schenk discloses the treatment of physiologically relevant peptides (but does not disclose or suggest the use of free-end specific antibodies in such treatment). For this reason, Examiners Chernyshev and Ulm agreed that those skilled in the art would not have been motivated to combine the teachings of Suzuki with those of Schenk.

The presence of the word "fragment" in the pending claims was discussed. Dr. Chain pointed out that the present invention covered the use of free-end specific antibodies that recognize physiologically relevant peptides. Thus, in certain embodiments, the antibodies called for in the claims bind any amyloid β-peptide or amyloid β-peptide fragment, provided the peptide or fragment includes the free-end epitope recognized by the antibody. For example, an antibody targeted to the free N-terminus of amyloid β-peptide (as called for, e.g., in claims 51 and 52) would recognize the free N-terminus of full-length amyloid β-peptides and would also recognize the free N-terminus of amyloid β-peptides that have been truncated at the C-terminus. Similarly, antibodies targeted to the free C-terminus of amyloid β-peptides Aβ1-39, Aβ1-40, Aβ1-41, Aβ1-42 or Aβ1-43 (as called for, e.g., in claims 63 and 64) would recognize the free C-termini of the respective amyloid β-peptides and would also recognize the respective free C-termini of Aβx-39, Aβx-40, Aβx-41, Aβx-42 or Aβx-43, i.e., amyloid beta peptides that have been truncated at the N-terminus. Examiners Chernyshev and Ulm indicated that this was one of the reasons that the prior art provided no motivation to combine the teachings of Suzuki and Schenk. It was agreed that deletion of the term "fragments" from the claims would overcome the obviousness rejection.

The claims have been amended along the lines agreed to at the interview. These amendments are believed to overcome the prior art rejections in the Office Action.

III. Claim rejections.

(i) Rejection Under 35 U.S.C. §102. In the Final Office Action, claims 14, 16-20, 22-25, 51, 52, 55, 56, 59, 60, 67 and 68 are rejected as anticipated by Schenk, WO 99/27944 ("Schenk").

The amended claims call for the presence of "free-end specific antibodies." As discussed during the interview (and as set forth in the Final Office Action) Schenk does not disclose free-end specific antibodies. Accordingly, for at least this reason, the rejection over Schenk is believed to have been overcome. For the record it is noted that the Examiner has indicated that certain claims in the present application are not supported in the specification of provisional patent application serial number 60/041,850 filed April 9, 1997 and therefore Schenk is prior art as to such claims. Although Applicants and their representatives do not agree with the Examiners' position, for the reasons outlined above, it is noted that the present claims are patentable over Schenk even if (*arguendo*) Schenk is prior art against the present claims.

(ii) Rejection Under 35 U.S.C. §103. Claims 63, 64, 71 and 72 have been rejected as obvious over Schenk in view of Suzuki, et al., U.S. Patent No. 5,750,349 ("Suzuki"). The Examiner contends that it would have been prima *facie obvious* to use the antibodies disclosed by Suzuki in a method of inhibiting amyloid β accumulation and neurotoxicity, as disclosed by Schenk.

As recognized by the Examiners during the interview (and as set forth in the Interview Summary above) those skilled in the art would not have been motivated to combine the teachings of Suzuki with those of Schenk, *i.e.,* even if Suzuki can be interpreted as disclosing free-end specific antibodies, those skilled in the art would not have been motivated to use such antibodies for treating the physiological peptides disclosed by Schenk. Accordingly, the present claims are not obvious over Suzuki and Schenk and this ground for rejection should be withdrawn.

IV. New Claims.

The present Amendment adds new claims 73-92. The new claims are directed to a method for inhibiting accumulation of amyloid β peptide in the brain or a method of inhibiting the neurotoxicity of amyloid β peptide. The new claims call for administering a free-end specific

antibody that is targeted to amyloid β peptide or an amyloid β peptide fragment truncated at position 3, 11 or 17.

New claims 77-88, 91 and 92 adopt the Examiners' suggestion that amyloid β-peptide fragments recited in the claims be physiologically relevant. Claims 77-88, 91 and 92 are directed to methods that call for administering a free-end specific antibody which is targeted to an amyloid β peptide fragment truncated at position 3, 11 or 17. These truncated amyloid β peptide fragments are physiologically relevant. *See* specification at page 8, paragraph [0031].

The new claims are patentable over the prior art of record. As discussed above, Schenk fails to disclose or suggest a free-end specific antibody to a physiologically relevant amyloid β peptide fragment. Thus, there would have been no motivation to combine Schenk with Suzuki to arrive at the methods claimed in the new claims.

For at least the reasons set forth above, new claims 73-92 are patentable over the prior art of record. Allowance of claims 73-92 is requested.

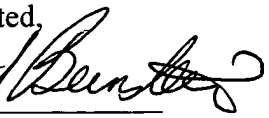
CONCLUSION

This application is believed to be in condition for allowance, which is earnestly solicited.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact Applicant's representative at the telephone number indicated below.

Dated: January 10, 2006

Respectfully submitted,

By 

Mitchell Bernstein, Ph.D.
Registration No.: 46,550
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant